Frequency, Disability Must Guide Migraine Prophylaxis

BY BRUCE K. DIXON
Chicago Bureau

SCOTTSDALE, ARIZ. — Monitor patients' headache frequency and disability to guide the pharamacologic prevention of migraine, Dr. Stewart J. Tepper said at a symposium sponsored by the American Headache Society.

"The goal should be to decrease migraine frequency by half and decrease duration and intensity, and comorbid illnesses are the critical aspect in picking the correct drug," said Dr. Tepper, director of the New England Center for Headache, New Haven, Conn.

Disability is as important in daily pharmacologic prevention as it is in acute treatment, and is the key to assessing therapeutic need, said Dr. Tepper, who is also with Yale University.

Circumstances that might warrant preventive treatment include:

- Frequent or infrequent migraine that significantly interferes with the patient's daily routine despite acute treatment.
- Failure of, contraindication to, or troublesome side effects from acute medications.
- Special circumstances, including hemiplegic migraine and attacks with a risk of permanent neurologic injury.
- Pattern of increasing attacks over time, with the risk of developing rebound headache with medicines for acute attack.
- Patient preference (the desire to have as few acute attacks as possible).
- Pregnancy with severe, disabling attacks accompanied by nausea, vomiting, and possibly dehydration.

Before choosing your approach, ask about family clinical response to specific medications. "If you have family members with success using propranolol, that's helpful because they're chips off the old block genetically," Dr. Tepper said.

He also emphasized the importance of using the lowest dose possible of a long-acting formulation and giving each treatment an adequate trial.

"It's critically important that you look for a pharmacologic twofer. … You want to treat comorbid illnesses while avoiding contraindicated medications," he said. "And the patient diary is a must if you want to make sure your outcomes are met."

The U.S. Headache Consortium guidelines, now in the process of revision, classify preventive migraine medications on the strength of scientific evidence from randomized, controlled trials in descending order from most evidence to least (A, B, or C) and by groups of effectiveness, 1 being most efficacious and 3 the least.

In group 1, class A drugs include the antiepilepsy drugs divalproex sodium and topiramate. Both drugs are associated with significant side effects, and divalproex use is limited by its propensity to cause birth defects and polycystic ovaries.

"We should not be using divalproex as first-line therapy in women of childbearing age," Dr. Tepper said, adding that patients offered topiramate should be warned about the risk of paresthesias and of reversible angle-closure glaucoma. "When patients develop paresthesias, I find that potassium supplementation is helpful."

The group 2 antiepilepsy drug gabapentin is class B but has not received Food and Drug Administration approval for migraine prevention. All three medications in this class produced modest reductions in migraine attacks in clinical trials. Gabapentin, which produced its best results at a dose of 2,400 mg, had a high dropout rate due to dizziness and drowsiness, he said.

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Included on the consortium's group 1 list are five alternative medications, of which three—chelated magnesium, riboflavin, and feverfew—are listed as class B. However, feverfew may be dropped from class B in the revision because of bad showings in two randomized, controlled trials.

The revision is also expected to include butterbur root and coenzyme Q10 in class B, Dr. Tepper noted.

Tricyclic antidepressants are clearly the standard when there are such comorbid illnesses as insomnia, neck pain, and depression, he said.

"Amitriptyline is a class A drug in group 1 but is not FDA approved for this indication. The other tricyclics are all class C in the guidelines, but since the guidelines were released there have been two small randomized, controlled trials of venlafaxine showing effectiveness in episodic migraine at a dose of 150 mg."

Dr. Tepper predicts that selective serotonin reuptake inhibitors, currently listed as class B and C medications, will be demoted in the revised guidelines.

"And I don't list botulinum neurotoxin type A because the evidence has shown ineffectiveness in episodic migraine, and studies are pending in chronic migraine," he added.

Two β-blockers, which Dr. Tepper prescribes for comorbid anxiety and hypertension, have been approved for episodic migraine prevention: Propranolol and timolol both have class A evidence and lie in group 1.

All of the calcium channel blocking agents available in the United States have class B scientific evidence. Calcium channel blockers are the drugs of choice for hemiplegic migraine and basilar-type migraine, Dr. Tepper explained.

Dr. Tepper disclosed significant relationships with Valeant Pharmaceuticals, Pfizer, Alexa, AstraZeneca, Endo Pharmaceuticals, and Eisai as the recipient of research grants; with Allergan Inc. as a consultant, lecturer, and recipient of research grants; with Johnson and Johnson as a lecturer and recipient of research grants; and with Merck U.S. Human Health as a consultant and recipient of research grants. ■

Topiramate Could Reduce Pediatric Migraine Frequency

BY MICHELE G. SULLIVAN
Mid-Atlantic Bureau

PITTSBURGH — Topiramate appears to be a good choice for preventing pediatric migraine, including basilar migraine, researchers reported at the annual meeting of the Child Neurology Society.

The drug was approved for treatment of adult migraine in 2004, and is used off label for pediatric migraine, said Dr. Marcus Cruz of St. Christopher's Hospital for Children, Philadelphia. "However, the availability of sufficient data to support the effectiveness, tolerability, and adequate dose is scarce and not yet well supported," he said.

Dr. Cruz retrospectively examined the use of topiramate as a migraine prophylactic in 37 children (mean age 14 years). Most of the group (81%) experienced migraine without aura; 11% had migraine with aura, and the rest of the children had abdominal, ophthalmoplegic, or catamenial migraine.

For 21 patients, topiramate was the first-line prophylactic therapy; for the rest, it was an add-on drug.

Most of the children (65%) had an excellent or good response to topiramate. Before treatment, the children had an average of 15 headaches per month; after treatment, that number decreased to about three per month.

Eight children had side effects, including cognitive effects (four), drowsiness (three), and paresthesias (one). All four patients who experienced cognitive side effects were switched to another medication. There was a direct correlation between dosage and side effects, Dr. Cruz noted. Children taking more than 2 mg/kg per day were significantly more likely to have adverse effects than were children taking less than 2 mg/kg per day.

Topiramate is also effective in preventing basilar-type migraine in children, said Dr. Donald Lewis, of Eastern Virginia Medical School, Norfolk. In a small, parallel-group study, the drug significantly reduced the total number of headache days per month, although it did not affect the duration or pain level of any headaches that still occurred.

Basilar migraine affects up to 19% of children with migraine, and is characterized by episodes of intense dizziness, vertigo, visual disturbances, ataxia, and diplopia, followed by pain.

Dr. Lewis' study included 14 children aged 6-18 years who received either 25 mg or 100 mg of topiramate per day. At baseline, the children had a median of five migraines per month.

After reaching their target dosage and entering a maintenance phase, 100% of children in the 25-mg/day group and 71% of those in the 100-mg/day group experienced a reduction in all migraine days of at least 50% per month (a median decrease from 4.5 days to 1.5 days), Dr. Lewis said.

The drug also significantly reduced the number of days with basilar migraines in each group from a median of 3 days to 0.6 days per month. Neither dosage had a significant effect on the duration or intensity of any migraines that occurred during treatment, however.

The study was supported by a research grant from Ortho-McNeil Neurologics Inc. ■

Gabapentin May Ease Symptoms In Patients With Fibromyalgia

WASHINGTON — Gabapentin brought greater relief of symptoms to patients with primary fibromyalgia than placebo in a randomized, double-blind trial, Dr. Lesley M. Arnold reported at the annual meeting of the American College of Rheumatology.

Gabapentin is known to be effective for neuropathic pain conditions, and growing evidence suggests fibromyalgia might share some of the same pathogenic mechanisms, said Dr. Arnold of the department of psychiatry at the University of Cincinnati.

The trial of 150 patients involved a 60-day phase when other psychotropic, sleep, and pain medications (besides over-the-counter NSAIDs and acetaminophen) were not allowed, a 6-week acute therapy phase when the dosage was titrated to 1,200-2,400 mg/day, and a 6-week stable dosage phase.

At week 12, the 75 gabapentin-treated patients had a significantly greater mean improvement on the Brief Pain Inventory (BPI) 24-hour average pain severity score than did the 75 placebo patients; this was the primary outcome of the study. Gabapentin-treated patients scored an average of 0.92 less on that inventory than did placebo patients. The BPI 24-hour average pain severity score is measured on a range from 0 (no pain) to 10 (worst pain imaginable).

A significantly higher percentage of gabapentin patients responded to treatment than did placebo patients (51% vs. 31%).

Gabapentin also significantly improved measures of the interference and impact of symptoms on daily life and functioning, clinical impressions, and sleep. But the drug provided no significant changes in tender point threshold or relief of depressive symptoms, said Dr. Arnold, who disclosed that she has received research grants and consulting fees or other payments from Pfizer Inc., and has served on its speakers' bureau.

The trial was supported by the National Institutes of Health.

—Jeff Evans